The Knowledge Foundation's 2nd Annual International Conference

BIOCHIPS 2002

Technology Development & Application

March, 18-20, 2002 • Crowne Plaza Richmond • Richmond, VA USA

In it's 2nd year, this internationally recognized conference addresses the most recent achievements in biochip, biosensor, microarray, and bioinformatics technologies. Biochips 2002 meets the demands of academia, government, and industry with emphasis on the major challenges faced by biochip developers bringing their technologies to the marketplace.

This conference will provide a balanced review of medical, biological and biodetection applications of biochip related instruments as well as examine the state-of-the-art technology R&D issues including:

Biochips in Perspective: Technology, Biology, Informatics

DNA and Protein Biochips

Multi-Functional Biochips for Biological and Medical Diagnostics

Advanced Detection and Sampling

On-Chip Monitoring of Cell Based Reactions

Biosensing - Silicon-Based Biosensors

Membranes, Microflows and In Vivo Monitoring

Microchip Platform for DNA Hybridization

Microelectronic DNA Array Devices for Molecular Diagnostics

Implantable Microchips for Drug Delivery

Microfluidic Systems - A Practical Perspective

Advanced Microarray Technologies for Genomics and Proteomics

Dissecting Gene Regulatory Networks

Oligonucleotide Arrays for Functional Genomics

Novel Automated Microarray Systems and Devices

Conveniently Timed
Biochips 2002
Hands-on-Workshop

Technologies for Producing and Analyzing High Density DNA Microarrays

March 20, 2002 • Virginia Commonwealth University Richmond, VA, USA

Organized by Virginia Commonwealth University's Center for Bioelectronics, Biosensors and Biochips (C3B) and Virginia Microelectronics Center (VMC)

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Monday, March 18, 2002

8:00 Registration, Poster/Exhibit Set-Up, Coffee and Pastries

TECHNOLOGIES AND PERSPECTIVES

8:50 Chairperson's Opening Remarks

Michael J. Heller, PhD, Professor, Depts Bioengineering/ Electronic and Computer Engineering, University of California San Diego; Consultant, Nanogen Inc.

9:00 KEYNOTE ADDRESS: BioChips in Perspective: Technology, Biology and Informatics

John N. Weinstein, MD, PhD, Senior Investigator, Laboratory of Molecular Pharmacology, National Cancer Institute, NIH

BioChips will revolutionize the biomedical sciences. That much is a universal assumption - or at least an urban legend. But the lofty expectations will be met only if we can overcome a number of major challenges - at the levels of technology, statistical analysis, and biological interpretation. In no context are those challenges as fully evident as in the application of BioChips to molecular pharmacology and drug discovery.

9:45 A Multi-Functional Biochip for Biological and Medical Diagnostics

Tuan Vo-Dinh, PhD, Group Leader, Corporate Fellow, Advanced Monitoring Development Group, Oak Ridge National Laboratory

We describe an integrated Multi-Functional Biochip (MFB), which allows simultaneous detection of several disease end-points using different bioreceptors such as DNA, antibodies, and enzymes on a single platform. The MFB includes an integrated circuit (IC) electro-optic system for the microchip detection elements based on the complementary metal oxide silicon (CMOS) technology. With this technology, highly integrated biochips are made possible partly through the capability of fabricating multiple optical sensing elements and microelectronics on a single system. The MFB device is a self-contained system based on an integrated circuit including photodiode sensor arrays, electronics, amplifiers, discriminators and logic circuitry on board. The highly integrated biochip is produced using the capability of fabricating multiple optical sensing elements and microelectronics on a single IC. The capability and potential of the biochip technology in medical diagnostics and biological pathogen monitoring will be discussed.

10:20 Refreshment Break, Exhibit/Poster Viewing

11:00 Dissecting Gene Regulatory Networks: A Two-Sided Approach

Thomas L. Volkert, Director, Whitehead Institute Center for Microarray Technology, Whitehead Institute

Much has been learned from microarray technology about how cells respond to environmental stimuli by regulating the expression of various genes. While this expression information is extremely useful for many purposes, it tells us very little about the underlying mechanisms that regulate gene expression. A global view of transcriptional regulation can only be obtained by integrating expression data with assays that directly monitor the activity of the transcription factors that regulate expression. Our goal is to create a network map for transcriptional regulation in yeast by combining expression analysis with transcription factor binding information from Genome-Wide Location Analysis. This talk will present the technique of Genome-Wide Location Analysis and show how it can be used to create network maps for transcriptional regulation.

11:35 A Microchip Platform for DNA Hybridization in Point-of-Concern DNA Diagnostics

Anthony Guiseppi-Elie, ScD, President and Scientific Director, ABTECH Scientific Inc.; Professor, Dept Chemical Engineering; Director, Center for Bioelectronics, Biosensors and Biochips, Virginia Commonwealth University

A microlithographically fabricated device or biochip platform has been developed for impedimetric and / or amperometric detection of DNA hybridization reactions. The microchip platform consists of a 32-element array of interdigitated electrodes or a 64-element array of microbore electrodes on oxidized silicon or glass. With 5 micron critical dimensions, this platform allows bioelectronic detection of DNA hybridization reactions performed on sensory elements. These elements allow: 1) label-free impedimetric detection of DNA hybridization, 2) enhanced impedimetric detection using colloidal gold nanoparticles that serve as labels of target DNA, and 3) the use of an electroactive layer of inherently conductive polypyrrole to provide for covalent attachment of DNA probes as well as to provide enhanced redox detection sensitivity with electroactive labels such as ferrocene. This biochip platform has enabled a whole new class of DNA diagnostic devices that are independent of fluorescence and have the potential for clinical diagnostics of targeted genetically-based conditions.

12:10 Implantable Microchips for Drug Delivery

Norman Sheppard, PhD, Director of Basic Research, MicroCHIPS, Inc.

Microfabrication technology is enabling the creation of intelligent drug delivery systems. Typical microchip systems include an array of sealed micro-reservoirs, where each reservoir is filled with a chemical and can be released on demand. Our group was the first to demonstrate the storage and in vitro release of multiple chemicals from a microchip, and recently, we achieved in vivo chemical release from subcutaneously implanted microchip devices. This talk will cover recent progress in the development of implantable microchips for drug delivery applications.

12:45 Speaker Power Luncheon Sponsored by The Knowledge Foundation

Don't miss an opportunity to meet one-on-one with our conference faculty. Delegates are invited to join participating speakers over luncheon to discuss today's "hot topic" biochip issues.

2:00 Chairperson's Remarks

Tuan Vo-Dinh, PhD, Group Leader, Corporate Fellow, Advanced Monitoring Development Group, Oak Ridge National Laboratory

APPLICATIONS

2:05 Advanced Detection Technologies

Alan S. Rudolph, PhD, MBA, Program Manager, Defense Sciences Office, DARPA

The Defense Advanced Research Projects Agency has explored innovative detection technologies for evaluating chemical and biological agent threats in environmental or medical diagnostic applications. These efforts include interfacing with biomolecular, cellular, tissue, and organismal-based systems in order to create technologies, which can rapidly assess threats, present correlative data on human health risk assessments. Specific examples of projects from the portfolio will be presented with the purpose of demonstrating both near term and next generation capability for enhancing our response to national security threats.

2:40 BioChips - Sampling and Detection in the Field

William Ragland, PhD, MBA, PE, Senior Account Manager, Life Sciences, Argonne National Laboratory

Many BioChip systems developed to date have been designed for use in "clean" industries: pharmaceutical screening, medical applications, and basic research. As applications of BioChips in field settings develop, BioChips systems will not only be used in a controlled laboratory environment but against the background noise of the biosphere. Such uses will require low cost, rugged systems with high discrimination than can be used either by operators with limited training or in an automated mode. Argonne National Laboratory, working with DOE, DARPA, other defense agencies, and several commercial partners, has been working for a number of years to develop a low cost, portable system to meet such these requirements. In optical detection, Argonne has already moved from the paradigm of putting the camera on the microscope to putting the microscope on the camera and, finally, to replacing the camera with CCD detection. Argonne's most recent hand-held microscope eliminates costly stages and focusing requirements. Argonne is testing its hand-held microscope for cross-platform compatibility with BioChips in addition to Argonne's MagicChip®. In developing cross-platform compatibility it is Argonne's goal to enable the use of BioChips from multiple sources for field use in areas such as environmental monitoring, food safety testing, and biodiversity research.

3:15 Microelectronic DNA Array Devices for Molecular Diagnostic, Pharmacogenomic and Other Applications

Michael J. Heller, PhD, Professor, Depts Bioengineering/ Electronic and Computer Engineering, University of California San Diego; Consultant, Nanogen Inc.

Active microelectronic array devices have been developed for applications in DNA diagnostics and pharmacogenomics research. Electronic hybridization formats provide considerable advantages for carrying out rapid SNP, point mutation and STR analysis with extremely high accuracy and reliability. Results from many thousands of test samples show that electronic hybridization provides higher reliability for homozygous and heterozygous calls than conventional "gold standard" methods (DNA sequencing, passive array, RFLP, etc.). Electronic hybridization allows highly reliable results to be obtained for problematic or difficult SNP's, which include SNP's with associated secondary structure, SNP's within

high G/C sequences and multiple SNP's in close proximity. High reliability minimizes the potential for false positives or false negatives, which will be an important performance criterion for any genotype panel that would be used for actual clinical diagnostic applications. In other areas, prototype integrated "sample to answer" systems are being developed for potential point of care and biohazard detection applications. These integrated systems can carry out cell separation, lysis, DNA/RNA extraction, amplification and genotyping (via electronic array hybridization).

3:50 Refreshment Break, Exhibit/Poster Viewing

MICROARRAYS - I

4:30 Demonstration of a Single-Color Expression Profiling Assay Based on Oligonucleotide Microarrays with a Three-Dimensional Polymeric Surface

Abhijit "Ron" Mazumder, PhD, Senior Manager, Expression Profiling, Motorola Life Sciences

The use of a three-dimensional, branched polymeric substrate, an integrated hybridization chamber which permits efficient mixing, and piezoelectric printing has generated a highly sensitive, specific, and reproducible expression profiling platform. The attachment chemistry permits the assay to be performed in probe excess, generating a linear dynamic range of 2.5 logs. A linear, sensitive, and reproducible detection method has generated a sensitivity of one copy per cell and CVs in the hybridization signals in the 7-12% range. The use of 30mer oligonucleotides permits the discrimination of sequences which are up to 90% homologous. Lastly, automation of the target preparation and batch processing of the slides generates low target preparation variability and high throughputs.

5:05 Development of Oligonucleotide Arrays for Functional Genomics

Viktor Stolc, PhD, Research Scientist, Center for Nanotechnology, NASA Ames Research Center

NASA Ames Research Center, Center for Nanotechnology (Moffett Field, CA) is developing functional genomics assays using high-density oligonucleotide arrays synthesized with electrochemistry. A high-density DNA-chip based method called quantitative phenotypic analysis is used to investigate the biological functions of all genes in yeast Saccharomyces cerevisiae under any growth condition. Yeast is used as a model system because it is one of the most genetically and genomically tractable organisms and because it has proven itself a model for the study of human physiology and genetics. http://ipt.arc.nasa.gov/stolc.html

5:40 SNP Analysis Using Surface Invasive Cleavage Reactions on Addressed Arrays

Michael R. Shortreed, PhD, Assistant Scientist, Dept Chemistry, University of Wisconsin-Madison*

The structure-specific invasive cleavage of single-stranded DNA by 5' nucleases is a useful means for sensitive detection of single-nucleotide polymorphisms or SNPs. The solution-phase invasive cleavage reaction has sufficient sensitivity for direct detection of as few as 600 target molecules with no prior target amplification. Our approach to the parallelization of SNP analysis is to adapt the invasive cleavage reaction to an addressed array format. Reverse fluorescence resonance energy transfer (FRET) was utilized for detection on first generation arrays. The second generation arrays, now in development, will employ label-free probes and use surface plasmon resonance (SPR) imaging for array readout. *In collaboration with: T. Berggren, R. Corn, M. Lu, L.M. Smith, and L. Wang, University of Wisconsin-Madison; J.G. Hall, V. Lyamichev, and B. Neri, Third Wave Technologies; P.W. Stevens and D.M. Kelso, Northwestern University

6:15 End of Day One

Tuesday, March 19, 2002

8:00 Exhibit/Poster Viewing, Coffee and Pastries

8:55 Chairperson's Remarks

Norman Sheppard, PhD, Director of Basic Research, MicroCHIPS, Inc.

BIOSENSING

9:00 Membranes, Microflows and In Vivo Monitoring

Pankaj Vadgama, PhD, Professor, Director IRC in Biomedical Materials, Queen Mary & Westfield College, United Kingdom

Any interfacing biosensor requires surface modification or membrane materials that create an interphase to modify the biomatrix compatibility of a device and control solute transport. Our work on solute selective thin and thick films will be described, capable of selective transport. Also work on porous membrane structures modified with pre-absorbed protein will be presented to assess their ability to permit lateral transport of indicator and binding proteins for electrochemical immuno detection. Thus description of solute flows will extend to flow in linear channels, where parallel, but non-mixed, electrolyte streams are shown to present a mobile barrier interphase serving to protect electrode surfaces. The concept of fluid flows to reduce electrode fouling will be extended to the case of percutaneously implanted metabolite sensors to permit reliable operation in a complex tissue environment.

9:35 Silicon-Based Biosensors

Philippe M. Fauchet, PhD, Professor, Director, Center for Future Health, University of Rochester

Silicon technology is very mature but it is only recently that biosensors made in and of silicon have been proposed. This presentation will review progress toward making optical and electrical silicon biosensors, including DNA sensors, protein sensors and bacteria sensors. These sensors rely on the simultaneous control of multiple length scales, from the nanometer to the micrometer level. The integration of these biosensors with silicon microelectronics will be discussed.

10:10 Refreshment Break, Exhibit/Poster Viewing

MICROFLUIDICS

10:45 Development of Microfluidic Systems - A Practical Perspective

M. Allen Northrup, PhD, President and CEO, Microfluidics Systems Inc.

In this presentation, we will present the practical view of microfluidic systems development, implementation and commercial opportunities. Examples will be given for automated sample processing for nucleic-acid-based pathogen detection. Included will be results from actual field trials and large volume water sample processing. As well, we will discuss the extension of these results and designs into system concepts and developments for applications such as oligonucleotide hybridization arrays. Issues concerning fluid handling, volumes, processing steps, and analytical methodologies will be presented. The perspective presented in this talk includes an analysis of existing commercial approaches and new research and development opportunities in the area of microfluidics.

11:20 On-Chip Monitoring of Cell-Based Reaction by Controlled Concentration Gradients

Michael M. Yang, PhD, Director, Applied Research Centre for Genomics Technology, City University of Hong Kong*

This presentation describes a passive microfluidics with simple planar geometry for mammalian cell-based reaction analysis. In order to reduce fabrication complexity, all functions were performed with a 2D main feature design with no moving parts employed. Fluidic flow is generated from liquid level difference among vials without the need for mechanical or electrical fluidic driving force. Difference liquid level programs (LLP) can be assigned for different flow patterns. Cell docking, where mammalian cells were driven and aligned on a dam structure was performed by carefully controlled LLP. Dilution of interested analyte is performed with different LLP such that an on-chip analyte concentration gradient is established. An ATP-dependent calcium uptake reaction is utilized as a model to demonstrate the ability of this micro-device in looking for threshold ATP concentration of this reaction. *In collaboration with: Li Cheuk Wing, Yang Jun, City University of Hong Kong

GENE EXPRESSION

11:55 Advances in Using GeneChip® Technology for Expression Studies

Gianfranco de Feo, PhD, Program Manager, Genomic Collaborations, Affymetrix, Inc.

Abstract not available at time of print.

12:30 Lunch on Your Own

program continues on flap...

MICROARRAYS - II

2:00 Chairperson's Remarks

Anthony Guiseppi-Elie, ScD, President and Scientific Director, ABTECH Scientific Inc.; Professor, Dept Chemical Engineering; Director, Center for Bioelectronics, Biosensors and Biochips, Virginia Commonwealth University

2:05 The Development of Protein BioChips

Lawrence K. Cohen, PhD, President and CEO, Zyomyx, Inc.

While technological innovation has adapted the analysis of genetic material to a miniaturized format, the more delicate nature of protein structures has precluded the development of analogous devices for proteins. Protein microarrays have started to emerge recently based on new developments and integration efforts in advanced materials, protein engineering, and detection physics. (i) High-density protein microarrays for quantification of multiple proteins in complex mixtures, (ii) implementation of new surface chemistries for immobilization of exactly defined quantities of proteins on each spot while retaining the full activity of the protein, and (iii) using this platform for developing the multiplexed, microchip-based immunoassay to analyze expression levels of serum proteins will be discussed. Detection limits on this microassay are equal to commercial ELISA tests and reduce the sample volume by many orders of magnitude.

2:40 Packard's HydroGel™ Substrate as a Platform for Protein Microarray Applications

Robert A. Cavallo, PhD, Research Scientist, BioChip Ventures Division, Packard BioChip Technologies

Microarrays will revolutionize proteomics as they have the field of genomics. Because proteins are more sensitive to their environment than nucleic acids, substrate requirements are heightened for protein microarray applications. At Packard BioChip Technologies, we have developed HydroGel™ coated slides, featuring a 3-D substrate that offers several advantages over other substrates, including a high probe loading capacity, low background and a 3-D environment that seems to preserve protein functionality and accessibility. This platform has been used to develop fluorescence-based multiplexed assays.

3:15 Plastic Labcard™ Devices and eTag™ Assay Systems for Genomics and Proteomics

Z. Hugh Fan, PhD, Principal Scientist, ACLARA BioSciences Inc.

Modern genetic analysis and drug discovery depend increasingly on the rapid, parallel, and inexpensive analyses of large numbers of samples. To address these needs, ACLARA is developing low-cost plastic Labcard™ devices that employ modern lab-on-a-chip techniques for highly parallel analyses. In addition, ACLARA's proprietary eTag™ chemistry technology works synergistically with electrophoretic separation methodology to enable rapid and multiplexed detection of both proteomic and genomic targets in each sample. An overview on the capabilities of plastic microfluidic device arrays and the multiplexing power of eTag assay systems, as well as recent results and commercial applications, will be presented.

3:50 Refreshment Break, Exhibit/Poster Viewing

4:20 The 4D™ System: A Novel Automated Microarray System

Andrew J. O'Beirne, DrPH, President and CEO, MetriGenix, Inc.

The 4D™ System consists of a patented Flow-thru Chip™ contained within a microfluidic cartridge, an automated hybridization station, chemiluminescent detection, and data analysis software. The system has been used for gene expression profiling, SNP detection, quantitative protein analysis, and Enzymology applications. The 4D™ System has the performance characteristics required to meet the needs of high throughput screening as well as individualized patient care.

4:55 The Use of Multiple or Alternative Fluors in Microarray Research

Ernest S. Kawasaki, PhD, Director of Biological Applications Development, Packard BioScience

Microarrays are rapidly becoming an indispensable tool for gene expression analysis, SNP studies, and proteomic research. Fluorescent dyes conjugated to nucleic acids or proteins is the primary method by which the interaction of nucleic acids or proteins is detected on microarrays. Many labeling techniques are available for attaching fluors to probes, and these methods are being adapted to microarray research. We will describe several of these methods and present examples of their use.

5:30 General Discussion

Moderator - Anthony Guiseppi-Elie

6:00 Closing Remarks, End of Conference

Conveniently timed!

BIOCHIPS 2002 HANDS-ON-WORKSHOP

Technologies for Producing and Analyzing High Density DNA Microarrays

Wednesday, March 20, 2002, Richmond, VA, USA

Organized by Virginia Commonwealth University's Center for Bioelectronics, Biosensors and Biochips (C3B) and Virginia Microelectronics Center (VMC)

This workshop aims to present principles, current best practices and methodologies for DNA Microarray fabrication with emphasis on differential gene expression in cancer genomics. This workshop is scheduled for the third day following the two-day Knowledge Foundation's BioChips 2002 International Conference (March 18-19) to be held in Richmond, Virginia. The workshop will include targeted lectures as well as direct hands-on training in the C3B's Advanced Microarraying Facility.

WHO SHOULD ATTEND

Industrial scientists and engineers who are interested in developing and applying DNA microarraying techniques to issues in protein engineering, metabolic engineering, bioprocess monitoring and optimization, and biocatalysis screening.

Academic researchers who are preparing to establish their own facility and who seek direct evaluation of a complete facility.

Research managers responsible for R&D strategic planning who are interested in exploring the role and value of microarraying technologies in their development programs.

LECTURE TIPS AND HANDS-ON LABORATORY SESSIONS:

- Microarray printing using a Cartesian Technologies PixSys 5500 SQ
- Data Analysis using GeneSpring's Expression Analysis Software
- Microarray Imaging using Packard BioChips Scan Array 5000
- Liquid handling using a Packard Biochips MultiProbe II
- Clean room protocol for biochips and DNA microarrays

Number of seats is limited. Please register early!

WORKSHOP AGENDA

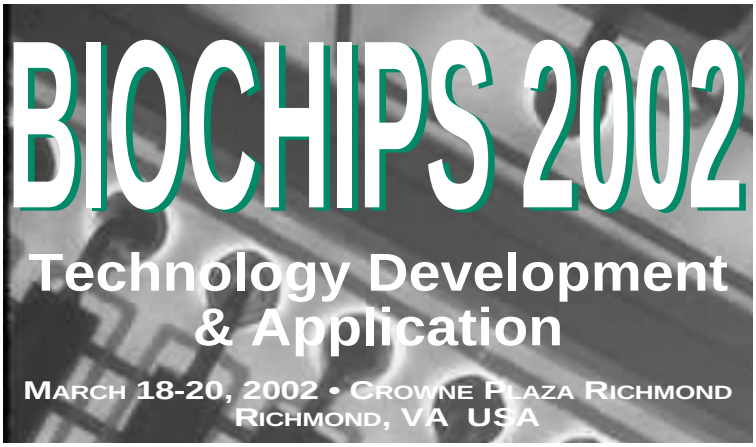
Rm. 105, School of Engineering Building,
601 West Main Street, Richmond, VA 23284

MORNING SESSION

7:30	Continental Breakfast
8:15	Welcoming Remarks
	Anthony Guiseppi-Elie
8:30	Biochip Fundamentals
9:00	Microarraying Techniques and Principles
	Cartesian Technologies
9:45	Array Scanning and Image Generation
	Packard Biochips
10:30	Coffee Break
10:45	Bioinformatics For Gene Expression Analysis Gene Spring
12:00	Lunch Break

AFTERNOON SESSION

1:00	Microarray Printing and Hybridization
2:00	Array Scanning and Image Generation
3:00	Date Visualization and Quantification
3:30	Informatics
5:00	Wrap-up
5:30	End of Workshop



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*The academic/government rate is extended to all participants registering as full time employees of government and universities. To receive the academic/government rate you must not be affiliated with any private organizations either as consultants or owners or part owners of businesses.

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Registration fee includes conference sponsored lunches, refreshments and all documentation made available to us by speakers. On-site registration is an additional $100. **Register in advance to secure your seat!**

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DISCOUNT ACCOMMODATIONS AND TRAVEL: A block of rooms has been allocated at a special reduced rate. Please make your reservations by **February 20, 2002**. When making reservations, please refer to the The Knowledge Foundation. Contact The Knowledge Foundation if you require assistance.

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Richmond, VA 23219

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SUBSTITUTIONS/CANCELLATIONS: A substitute member of your company may replace your attendance at any time at no charge if you find your schedule prevents you from attending. Please notify us immediately so that materials can be prepared. If you do not wish to substitute your registration, we regret that your cancellation will be subject to a $100 processing fee. To receive a prompt refund, we must receive your cancellation in writing 15 days prior to the conference. Unfortunately cancellations cannot be accepted after that date. In the event that The Knowledge Foundation, Inc. cancels an event, The Knowledge Foundation, Inc. cannot resume responsibility for any travel-related costs.

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You can purchase a full set of conference documentation. Simply check the box on the registration form and send it to us along with your payment. Please allow 4 weeks after the conference date for delivery.